

up version of the changes made to the amended Claims by the instant Amendment. The attached page is captioned "Version With Markings To Show Changes Made."


*Fees*

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

CONCLUSION

Applicants respectfully submit that the Claims as amended are believed to be in condition for allowance. Thus, early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

  
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**Version With Markings To Show Changes Made**

That which is underline is added, and that which is in brackets is removed.

**IN THE SPECIFICATION:**

Page 1, immediately below the title, please insert the following paragraph:

**PRIORITY CLAIM**

This application is a 35 U.S.C. § 371 filing of PCT Application number PCT/FR00/01594 filed on June 8, 2000, which claims the benefit of French Application number 99 07449 filed June 11, 1999.

**IN THE CLAIMS:**

1. (Amended) A defective recombinant adenovirus that is incapable of autonomously replicating, said defective recombinant adenovirus comprising[, characterized in that it comprises] at least one DNA sequence encoding the specific iodine transporter (Na<sup>+</sup>/I<sup>-</sup> Symporter) NIS or a derivative thereof, wherein said DNA sequence is placed under the control of a transcriptional promoter allowing its expression in tumor cells.
2. (Amended) The defective recombinant adenovirus of Claim 1, wherein [as claimed in claim 1, characterized in that] the DNA sequence is a cDNA sequence.
3. (Amended) The defective recombinant adenovirus of Claim 1, wherein [as claimed in claim 1, characterized in that] the DNA sequence is a gDNA sequence.
4. (Amended) The defective recombinant adenovirus of Claim 1, wherein [as claimed in

one of claims 1 to 3, characterized in that] the DNA sequence encodes the specific murine iodine transporter (Na<sup>+</sup>/I<sup>-</sup> Symporter) NIS.

5. (Amended) The defective recombinant adenovirus of Claim 1, wherein [as claimed in one of claims 1 to 3, characterized in that] the DNA sequence encodes the specific human iodine transporter (Na<sup>+</sup>/I<sup>-</sup> Symporter) NIS.

7. (Amended) The defective recombinant adenovirus of Claim 1, wherein [as claimed in claim 6, characterized in that] the transcriptional promoter is a viral promoter [is chosen from viral promoters, preferably from the promoters E1A, MLP, CMV and RSV-LTR, MT-1, SV40].

8. (Amended) A defective recombinant adenovirus that is incapable of autonomously replicating, said defective recombinant adenovirus comprising a cDNA sequence encoding the human iodine transporter NIS under the control of the CMV promoter.

9. (Amended) A defective recombinant adenovirus that is incapable of autonomously replicating, said defective recombinant adenovirus comprising a DNA sequence encoding the iodine transporter NIS or a derivative thereof under the control of a promoter allowing predominant expression in tumor cells.

10. (Amended) The defective recombinant adenovirus of Claim 9, wherein [as claimed in claim 9, characterized in that] the promoter is selected from the group consisting of [chosen

from] the regulatory sequence of the elastase I gene, the regulatory sequence of the insulin gene, the regulatory sequence of the gene for immunoglobulins, the regulatory gene of the mouse mammary tumor virus, the regulatory sequence of the PSA gene, the regulatory sequence of the alpha-fetoprotein gene, the regulatory sequence of the alpha 1-antitrypsin gene, the regulatory sequence of the  $\beta$ -globin gene, the regulatory sequence of the gene for basic myelin, the regulatory sequence of the gene for the myosin light chain 2, and the regulatory sequence of the gene for the gonadotrophin-releasing hormone.

11. (Amended) The defective recombinant adenovirus of Claim 1, further comprising [as claimed in one of claims 1 to 10, characterized in that it comprises at least] a deletion of all or part of an [the] E1 region, [and] a deletion of all or part of an [the] E4 region, or a deletion of all or part of the E1 region and a deletion of all or part of the E4 region.

13. (Amended) The defective recombinant adenovirus of Claim 1, wherein said adenovirus [as claimed in one of claims 1 to 12, characterized in that it] is a human adenovirus type Ad 2 or Ad 5 or a canine adenovirus type CAV-2.

14. (Amended) The defective recombinant adenovirus of Claim 1, further comprising [as claimed in one of claims 1 to 13, characterized in that it comprises, in addition,] at least one gene encoding a polypeptide involved in a peroxidase system [such as the gene for glucose oxidase or for thyroperoxidase].

15. (Amended) A pharmaceutical composition comprising said defective recombinant adenovirus of Claim 1 and a physiologically acceptable vehicle [The use of the adenovirus as claimed in one of claims 1 to 14, for the preparation of a pharmaceutical composition intended for treating and/or for inhibiting the growth of tumors].

17. (Amended) The pharmaceutical composition of Claim 15, [as claimed in claim 16, characterized in that it is] in injectable form.

18. (Amended) The pharmaceutical composition of Claim 15, comprising [as claimed in claim 16 or 17, characterized in that it comprises] between  $10^4$  and  $10^{14}$  pfu/ml[, and preferably  $10^6$  to  $10^{11}$  pfu/ml] defective recombinant adenoviruses, inclusive.